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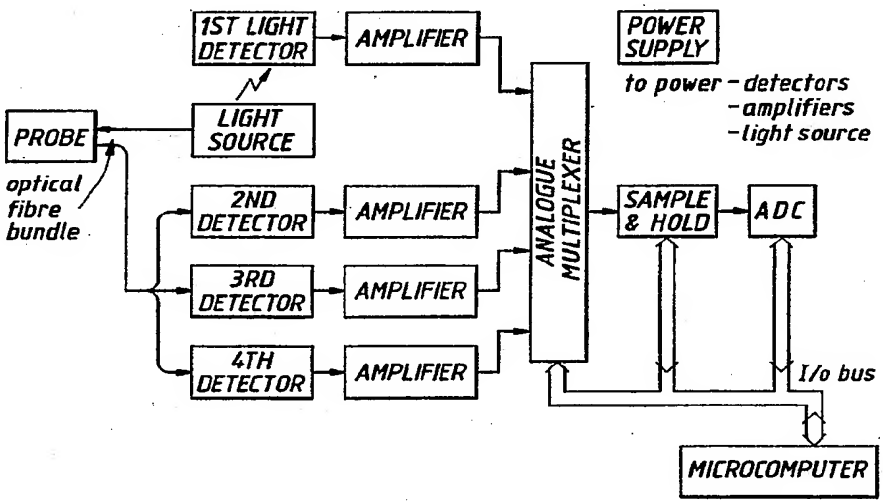

(57) Abstract

A system is disclosed for *in vivo* monitoring of the presence and concentration of meconium and/or blood in amniotic fluid. One aspect of the invention provides a non-invasive system for monitoring the content of amniotic fluid during labour which comprises an optical cell (31) supported in a probe (32) capable of insertion into the uterus during labour, said cell being connected optically to a source of light (having a suitable spectral bandwidth) and to photodetecting means for detecting the spectral response of the amniotic fluid to illumination with said source and processing means for determining the presence of meconium and/or blood in the amniotic fluid by analysis of the spectral response. The invention includes an intrauterine probe (32) which comprises a flexible elongated body and an optical cell (31) housed therein, the cell being optically connected by fibre optic cable (33) to the distal end and the cell being located in the housing so that in use amniotic fluid is able to pass through the cell.

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MECONIUM MONITORING SYSTEM

This application relates to a system and method for monitoring the quality of amniotic fluid during labour.

In recent years, it has become accepted that there is a need for more information concerning the condition within the uterus just prior to and during labour in order to predict and avoid birth complications. U.K. Patent Application No. 87 23605 (Publication No. 2195897) describes an intrauterine probe which enables certain conditions, especially the fetal heart rate and the intrauterine pressure to be continuously monitored during labour. Any monitoring system should desirably be non-invasive to the fetus and be capable of a continuous collection of data concerning the condition of interest.

During intrauterine life, the human fetus collects within its bowel a collection of debris known as meconium. Passage of meconium in utero occurs in about 10% of babies overall, probably as part of a sympathetic 'fright, flight or fight' reaction. Because regular uterine contractions interfere with maternal blood flow within the placenta, the mean oxygen tension in fetal blood during labour drops from about 5 to 3kPa. This is thought to be the major stimulus causing the fetus to pass meconium in utero; it occurs with increasing frequency as gestation advances, reaching almost one third of all fetuses by 42 weeks gestation.

In 90% of fetuses who pass meconium into the amniotic fluid there are no harmful effects. However, in about 10% of cases the fetus gasps, inhaling the sticky, particulate meconium into the upper respiratory tract. Once the baby is born, this particulate matter produces partial airways obstruction, leading to inability to inflate alveoli in some areas, and hyperinflation in others. This disease is known as meconium aspiration syndrome (MAS).

Attempts have been made to prevent MAS by careful suctioning of the baby's pharynx immediately after the head is delivered; unfortunately such measures are largely ineffective.

It appears that there is, as yet, no known effective prevention of this crippling and disabling condition. The main factor preventing progress is that the appearance of meconium into the amniotic fluid often remains undetected because the tight fit of the head in the pelvis does not allow amniotic fluid to drain out and become visible to the attending obstetrician.

There is therefore a need for a method of reliably monitoring the onset of meconium passage into the amniotic fluid and particularly one which can be carried out non-invasively to the fetus and continuously throughout labour.

According to one aspect of the present invention,

there is provided a non-invasive system for monitoring the content of amniotic fluid during labour which comprises an optical cell supported in a probe capable of insertion into the uterus during labour, said cell being connected optically to a source of light (having a suitable spectral bandwidth) and to photodetecting means for detecting the spectral response of the amniotic fluid to illumination with said source and processing means for determining the presence of meconium and/or blood in the amniotic fluid by analysis of the spectral response.

According to a second aspect of the present invention there is provided an intrauterine probe which comprises a flexible elongated body and an optical cell housed therein, the cell being optically connected by fibre optic cables to the distal end and the cell being located in the housing in such a way that in use amniotic fluid is able to pass through the cell.

Further features and advantages of the present invention will become apparent from the following detailed description and accompanying drawings in which:-

Figure 1 is an absorption spectrum of three samples A, B & C of different amniotic fluids.

Figure 2 is an absorption spectrum of a blood-stained sample of amniotic fluid with expected base line.

Figure 3 is a perspective diagrammatic view of an intrauterine probe in accordance with the invention.

Figure 4 is an exploded view of an optical cell on an enlarged scale.

Figure 5 is a block diagram illustrating the signal processing equipment.

Two difficulties in making direct observations of the absorption spectrum of amniotic fluid are first to differentiate the spectra for meconium and blood, and secondly, to take into account the differing overall opacities between different samples of amniotic fluid. Typical spectra are shown in Figure 1, where A is the spectrum of a sample clear of meconium and blood, whereas B is the spectrum of a meconium stained sample showing a strong absorption peak in the range of 405 to 415nm, and C that of a blood stained sample. It can be seen that spectrum C has a major peak in the range of 405 to 415nm and two minor peaks in the range 535 to 545nm and 570 to 580nm.

The effect of blood on the absorption spectrum is important as it affects the whole spectrum in the range 405 to 415nm, where it adds a wide band peak in the same way as meconium does, the main difference between the two spectra being the two peaks seen at 540 and 575nm, and the fact that meconium absorbs poorly above about 650nm.

In order to account for the different opacities and distinguish between clear, meconium or blood-stained

amniotic fluid, the system and method of the present invention involves a comparison of the spectral response at different wavelengths. One way in which this can be done is to measure the absorption spectrum of the amniotic fluid in the areas corresponding to the peaks produced by meconium and blood and at a third wavelength which is distant from the peaks characteristic of meconium and blood. In this way a base line value can be subtracted from the peak absorption values of the fluid under test. This procedure is illustrated graphically in Figure 2 which is a spectrum of a blood-stained sample of amniotic fluid containing meconium. It will be seen from Figure 2 that the point at 500nm can be taken as the base line. From these three absorptances we can derive the following variables:-

$$\delta(405) = K1 \cdot [\, A(405) - A(500) \,]$$

$$\delta(575) = K2 \cdot [\, A(500) - A(575) \,]$$

where : A(405) = absorptance at 405nm

A(500) = absorptance at 500nm

A(575) = absorptance at 575nm

These variables are referred to hereinafter as the compensated absorptances. K1 and K2 are arbitrary constants to bring both values in the range 0 to 1.

For a sample clear of meconium and blood, $\delta(405)$ and $\delta(575)$ are both positive. As the level of meconium is increased, both $\delta(405)$ and $\delta(575)$ should increase but in

the case where blood is also present, S(575) does not increase significantly and often decreases to become negative, this is because the addition to the spectrum of a peak at 575nm reduces the difference A(500)-A(575).

Therefore, should blood appear in the amniotic fluid when meconium is already present, blood would immediately be detected, which is important as the appearance of blood in the amniotic fluid is a life-threatening condition requiring immediate attention.

While absorptance measurements can be used to discriminate amniotic fluid containing meconium or blood and clear fluid, a perfectly normal amniotic fluid may be extremely turbid because of the presence of vernix (a waxy substance which covers the fetus). In such circumstances, the vernix contamination makes it difficult to obtain meaningful absorptance measurements, except possibly in very thin films or after removal of a sample and centrifugation to clear the sample. The latter procedure is not usually possible where continuous monitoring is required.

A preferred procedure for analysing the spectral response of the amniotic fluid to illumination involves measurement of light back scattered (i.e. reflected) from a sample of the fluid. An amniotic fluid which is contaminated with vernix has a milky appearance and reflects light strongly over a wide waveband. As meconium

increases in the amniotic fluid, it is also responsible for scattering light. Further, increased turbidity of the fluid will result in a reflected signal of increased strength.

It is, however, possible to distinguish increases in reflectance due to the presence of meconium, as opposed to vernix or other contaminants, by exploiting the optical absorptance characteristics of meconium as mentioned above. Because meconium absorbs light in the range of about 402 to 420nm, measurement of reflected values in this waveband compared with reflectance values at a wavelength where there is no significant absorption by meconium makes it possible to estimate the concentration of meconium. Observations have shown that light reflected from a sample of the fluid at 405 to 420nm increases with meconium concentration until a certain point (which is not necessarily the same from one sample to the next), where it starts to decrease due to the absorbing properties of meconium in that range. In contrast, reflectance values at, for example, 700nm continue to increase up to the maximum concentration measured (100g per litre of meconium). Blood can be differentiated in a similar way by measuring the reflectance at a third wavelength where blood absorbs light but meconium does not (540nm has been found to be suitable) and also at 700nm, where like meconium its

absorptance is small. Although Figure 1 may suggest at first sight that light absorptance by blood at 700nm is significant, the spectrum at 700nm is, in fact, the overall attenuation of a light beam due to both absorption and scattering of light. According to the Beer Lambert Law, the intensity I of a monochromatic light beam of initial intensity I_o passing through a medium of path length d and concentration c is:-

$$I = I_o e^{-ad}$$

where a is the attenuation coefficient which is plotted in Figures 1 and 2. The attenuation coefficient is, in fact, the sum of the absorption and scattering coefficients and is related to concentration of the substance under investigation in the following way:-

$$a = (a_1 + a_2)c$$

where a_1 is the absorption coefficient and a_2 is the scattering coefficient.

The scattering coefficient for blood is much larger than for meconium, but the absorption coefficients of both meconium and blood are insignificant at 700nm and can be ignored. Therefore, 700nm provides a suitable base line for concentration determinations when using reflectance measurements for both blood and meconium by logarithmic treatment of the reflectance measurements at 405 to 420nm, 540nm and 700 nm. Thus, by measuring the intensity of the illuminating light (and its spectral content), the

intensity of incident light at each wavelength of interest (e.g. 405-420, 540 & 700nm) can be calculated. Using these values and the values of reflected light at the same three wavelengths, the reflection due to the vernix content can be allowed for and compensated reflectance values calculated which are related to the content of meconium and blood in the amniotic fluid. From these compensated values, the concentration of meconium and blood can be calculated with a reasonable degree of accuracy.

Optical measurements can be conveniently made in vivo, using a flexible intrauterine probe of the kind described in British patent application No. 8723605 (Publication No. 2195897). This is illustrated diagrammatically in Figure 3. As described in our above application, the probe is moulded from a suitable plastics material such as polyurethane and is stiff and resilient enough to enable it to be inserted by pushing into the uterus from the proximate end through the cervix and around the fetal head. The shape and dimensions and mechanical properties of the body of the probe are preferably as described in UK Patent Specification No. 2195897, the disclosure of which is incorporated herein. Optical measurements are made using an optical cell which is encapsulated in a potting composition from which the probe is formed. The optical cell is preferably

constructed in such a way that fluid can flow from one side of the probe through to the other by passing through passages in the cell. Thus referring to Figure 3, the optical cell 31 is encapsulated in the body 32 of the probe and the cell is optically connected to an optic fibre bundle 33, also encapsulated in the body 32. Bundle 33 emerges from the proximate end of the probe from which it is optically connected (indicated diagrammatically in Figure 5) to photodetectors.

The cell is shown in Figure 4 and is manufactured in two inter-engaging parts (41 & 42). Figure 4 shows the cell in an exploded view. Part 42 includes a bore 43 (typically about 3mms in diameter), for receiving the fibre optic bundle 33 (not shown in Figure 4). The fibre optic bundle comprises a large number of optic fibres which are located in bore 43 and preferably sealed in place with a suitable thermoplastic resin, e.g. an epoxy resin to prevent ingress of amniotic fluid by capillary action. Suitable optic fibre bundles are supplied by Fibre Data Limited, Unit 8, Pool Industrial Estate, Druids Road, Redruth, Cornwall TR15 3RH. The particular fibre bundle employed contained about 540 silica fibres and was randomly divided into two equal branches (known as a 'Y' shape bifurcated bundle), one branch serves to transmit light into the optical cell and the other collects the reflected light and conveys it to the spectrophotometer,

comprising the photodetectors. When assembled, part 42 is secured to part 41 by the screws or studs indicated. Part 41 is shaped to provide conical or triangular-shaped counter-surfaces which prevent light which strikes such surfaces from being reflected back into the optic fibre-ends 45 of bore 43. Preferably, the internal faces 44 are coated with an anti-reflecting material or are roughened to minimise reflection.

When encapsulated in the material forming the body of the probe, faces 46 & 47 of parts 41 & 42 will be parallel with the flat surfaces 35 of the probe and flanges 48 & 48A of parts 41 & 42 will serve to lock the parts into the body of the probe. However, a passage 38 remains open through the probe and cell so that in use amniotic fluid may pass through the cell from one side of the probe to the other. Because the flat face 35 of the probe will in use lie against the wall of the uterus, light cannot be reflected from the uterus into the optic fibre bundle which is important since the wall of the uterus is red and would give a spurious signal.

Figure 5 shows a block diagram of the processing system. As illustrated in the block diagram, light from the source is fed to the probe via the optic fibre bundle and a first light detector is linked to the light source and measures its intensity. Reflected light is returned from the probe to second, third and fourth photodetectors

(which may be photodiodes) and are tuned to detect the reflectance values at the three wavelengths of interest, i.e. 405-420nm, 540nm, and 700nm, respectively. After amplification, the signals are fed via an analogue multiplexer and an analogue-digital converter to a microcomputer.

The light source used to illuminate the sample passing the optical cell may be any suitable light source of sufficient intensity at the three desired wavelengths.

Preferably, the light source is a tungsten halogen filament bulb, although any light source emitting light at 415, 540 and 700nm would be suitable. The tungsten halogen lamp has the advantage that, while the total intensity fluctuates with temperature, the spectral content remains constant. Thus, by measuring overall intensity, the intensity delivered at each of the three selected wavelengths can easily be calculated.

The optical components and electronics circuitry can be housed together in a box adjacent to the bed and linked to probe. The output from this box may be taken to a central processing unit such as a microcomputer via a suitable interface. This arrangement enables the compensated reflectances to be calculated automatically and in real time, logged and displayed on a VDU or any suitable display in terms of corresponding concentrations of meconium and blood, or a hard copy record to be

produced. Alternatively, a simpler read-out can be employed which merely gives an indication, when meconium and/or blood is detected at a level which suggests cause for alarm.

CLAIMS

1. A non-invasive system for monitoring the content of amniotic fluid during labour which comprises an optical cell supported in a probe capable of insertion into the uterus during labour, said cell being connected optically to a source of light (having a suitable spectral bandwidth) and to photodetecting means for detecting the spectral response of the amniotic fluid to illumination with said source and processing means for determining the presence of meconium and/or blood in the amniotic fluid by analysis of the spectral response.

2. A system according to claim 1 in which the cell is orientated in the probe in such a way that the amniotic fluid is illuminated by said light source while avoiding any reflection of light from the wall of the uterus reaching the photodetecting means.

3. A system according to claim 1 or claim 2 in which the optical cell is connected to the photodetecting means and to the light source by fibre optic cable.

4. A system according to claim 3 in which the fibre optic cable comprises a bundle of intermingled fibres, some of said fibres being optically connected at the end remote from the cell with the light source and others with the photodetecting means.

5. A system according to any one of the preceding claims in which the spectral response is analysed by

determining the light reflected at first and second wavelengths at which meconium and blood, respectively, strongly absorb light and at a third wavelength at which meconium and blood do not absorb light significantly.

6. A system according to claim 5 in which the first wavelength is about 405 to 420 nm, the second wavelength is about 540 nm and the third wavelength is about 700 nm.

7. An intrauterine probe which comprises a flexible elongated body and an optical cell housed therein, the cell being optically connected by fibre optic cable to the distal end and the cell being located in the housing so that in use amniotic fluid is able to pass through the cell.

8. A probe according to claim 7 wherein the interior of the cell is provided with non-reflecting surfaces.

9. A probe according to claim 7 or 8 in which the fibre optic cable comprises a bundle of fibres, some of the fibres serving to transmit light and others to convey light reflected by the amniotic fluid to the proximal end for detection by photodetecting means, the fibres which transmit light and the fibres which receive reflected light being intermingled in the bundle.

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FIG. 1.

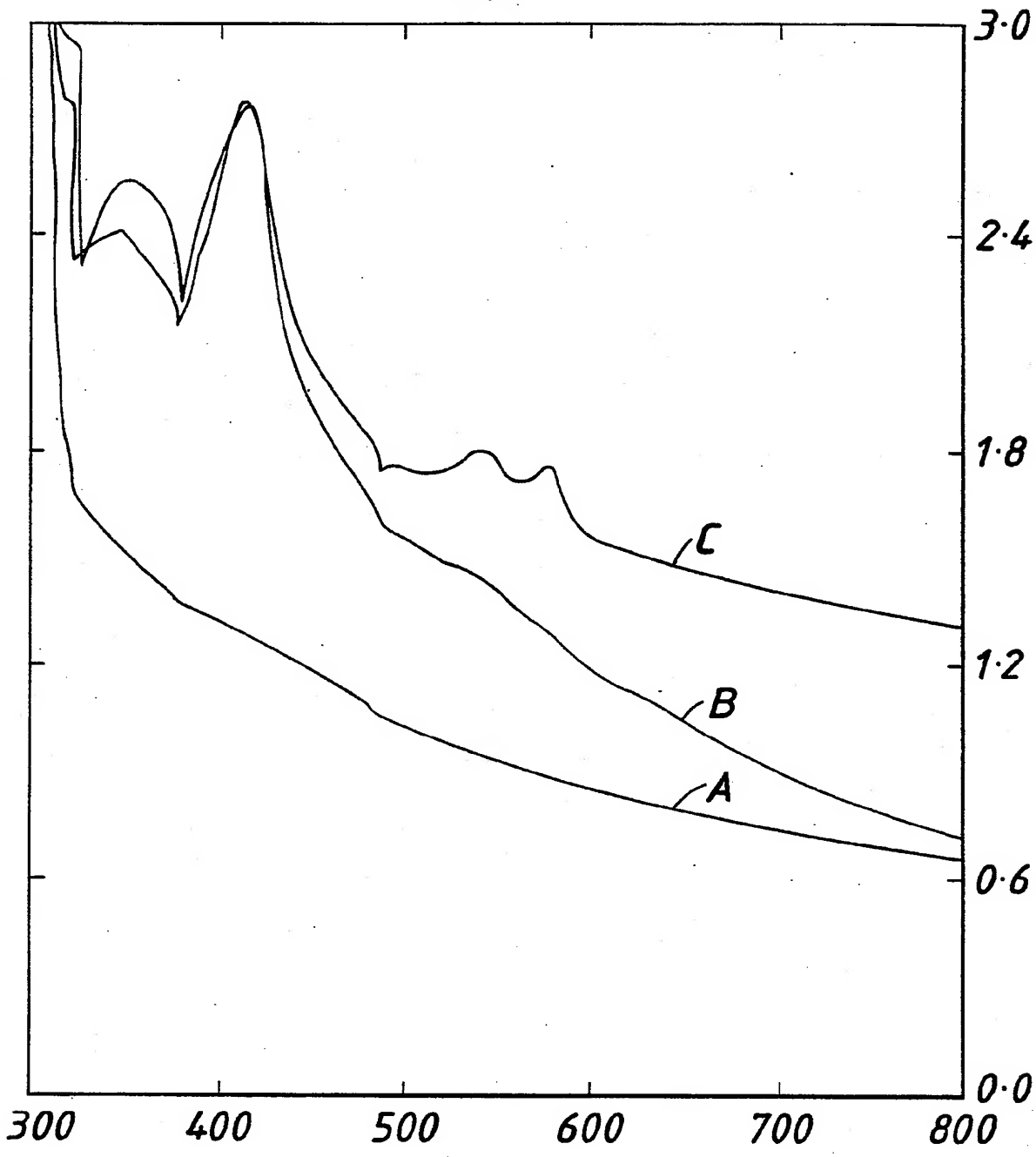
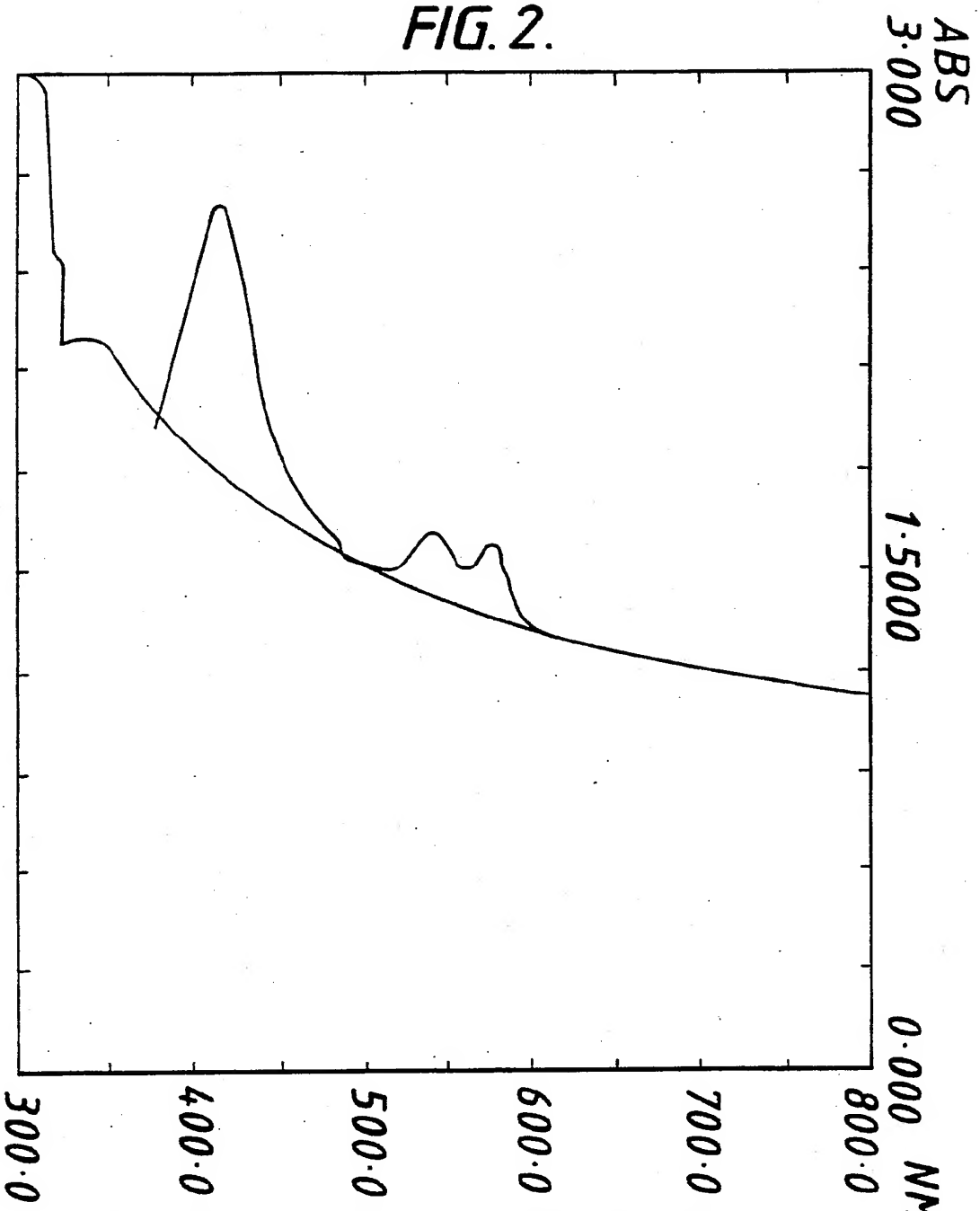


FIG. 2.



Blood stained amniotic fluid spectrum with expected baseline.

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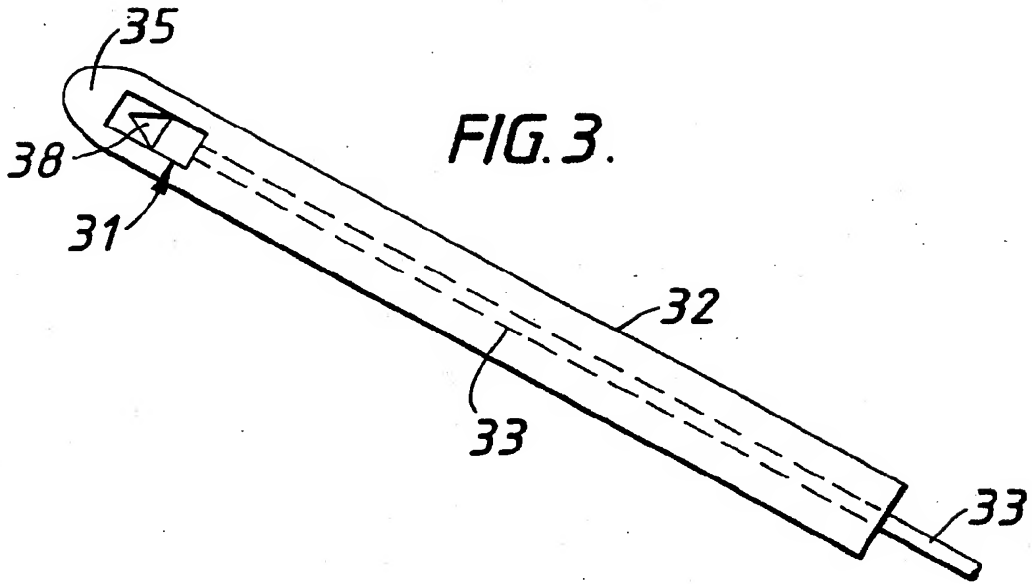
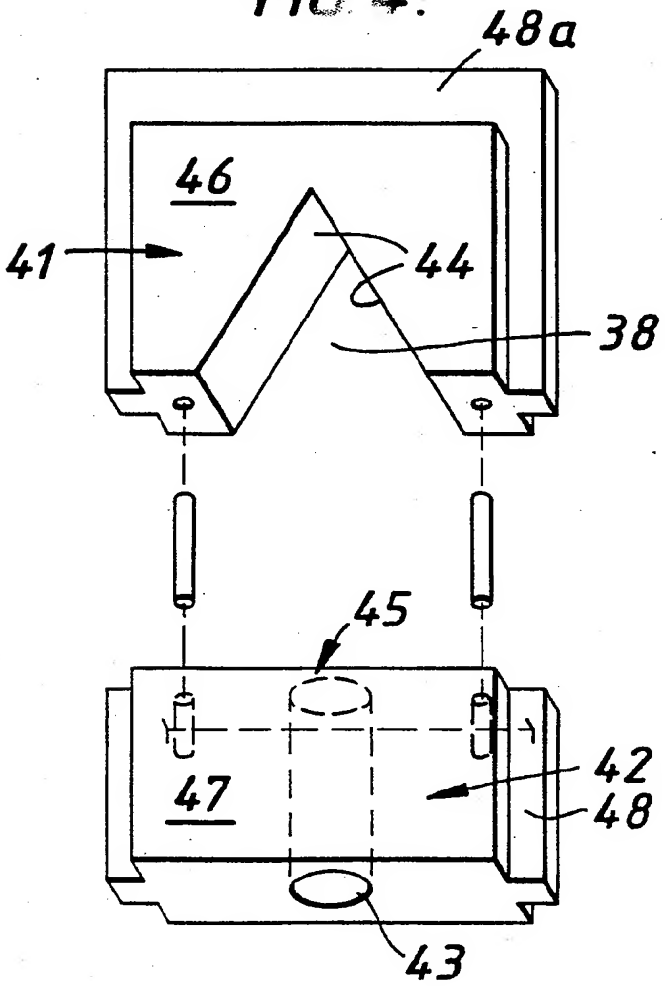
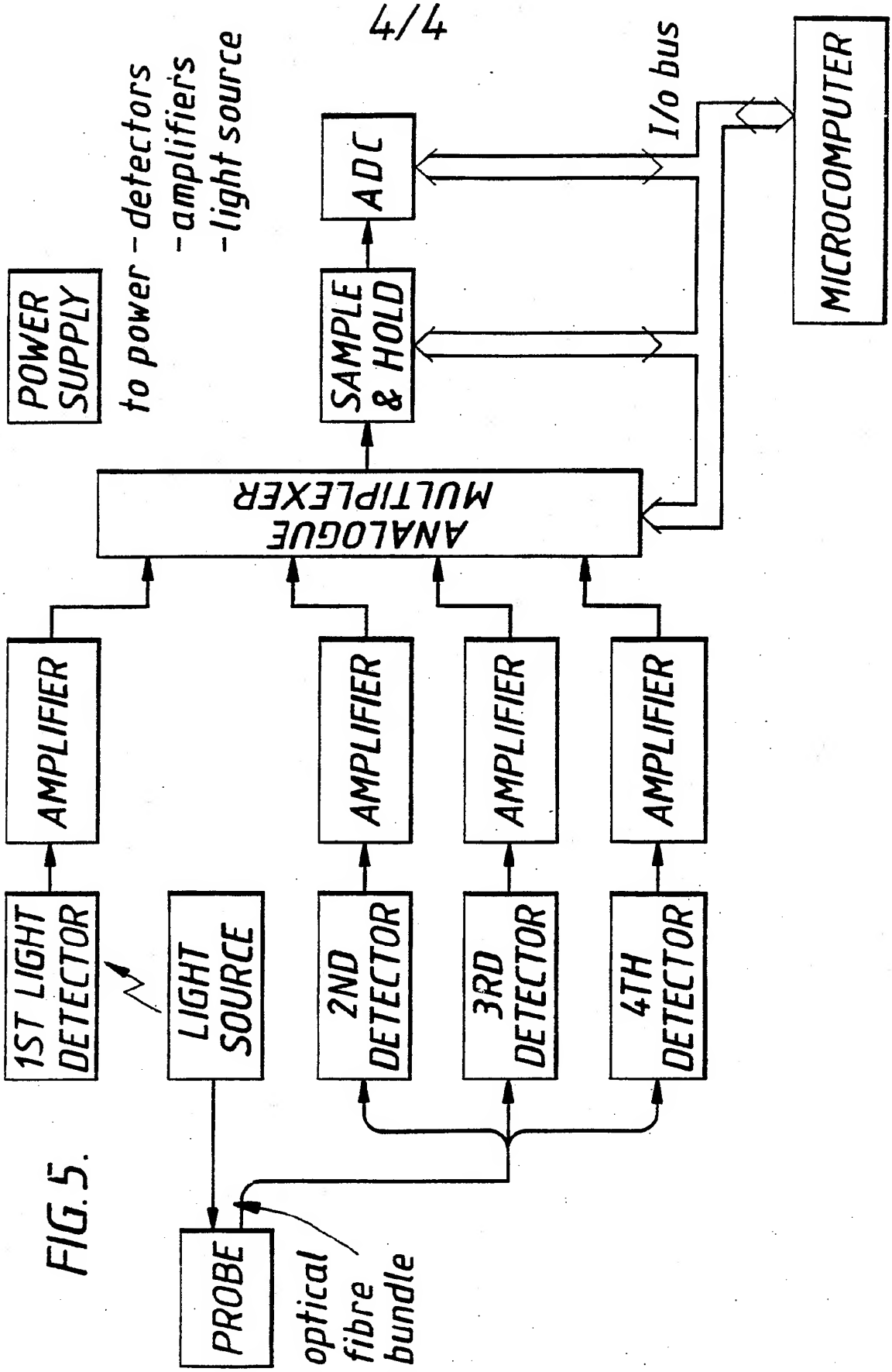


FIG. 3.

FIG. 4.

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- amplifiers
- light source
AMPLIFIER
AMPLIFIER
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AMPLIFIER
1ST LIGHT DETECTOR
LIGHT SOURCE
2ND DETECTOR
3RD DETECTOR
4TH DETECTOR
PROBE
optical fibre bundle

FIG. 5.

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 91/01090

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61B5/00

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	A61B

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
X A	FR,A,2 608 909 (G.KARCHER ET AL.) July 1, 1988 see the whole document	1 2-9
A	GB,A,2 195 897 (ST. MARY'S HOSPITAL MEDICAL SCHOOL) April 20, 1988 cited in the application see the whole document	7-9
A	EP,A,063 431 (M.KONOMI) October 27, 1982 see the whole document	1-9

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09 OCTOBER 1991	19 NOV 1991
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GB 9101090
SA 49250

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